

# It is about time physicians and clinical microbiologists in infectious diseases investigated the aetiology of obesity

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As we are in the middle of an unprecedented outbreak of obesity in the world, the role of the gut microbiota and its manipulation need to be investigated and our area of study needs to be involved in the process. Since 2006 [1] a link has been established between the composition of the gut microbiota and obesity. This has highlighted that the Firmicutes to Bacteroidetes ratio of the gut is different depending on the body weight and on the diet of people. Moreover, the transplantation of the gut microbiota from obese humans or mice to xenobiotic mice consistently modifies the mouse metabolism and induces a tendency to develop diabetes as well as a metabolic syndrome [2]. Data are accumulating that show that the gut microbiota repertoire is linked with both obesity and diet. The recent link observed between obesity and the composition of the human gut microbiota raises the hypothesis that the antibiotics and probiotics that manipulate the gut microbiota and that have been used in the farming industry as growth promoters for decades, may also cause weight gain in humans [3].

Antibiotics are still being used in the USA by the farming industry to promote weight gain in livestock. The same effect has been found in a recent study in laboratory mice receiving low doses of antibiotics (penicillin and vancomycin) and who subsequently showed weight and adiposity gain [4]. The composition of the mouse microbiota was changed during treatment. Interestingly there was a significant increase of Lactobacillales in the fecal samples of the antibiotic-treated mice. Another study has found that children receiving antibiotics before the age of 3 months are bigger than others [5]. In adult humans, some studies show weight gain following treatment with vancomycin [6]. For years, an equivalent to vancomycin was used as a growth promoter in farm animals, under the name of Avoparcin. Interestingly these compounds are active against most gram-positive bacteria except for some *Lactobacillus* species [6]. Finally, there is evidence that patients with prolonged antibiotic treatment for *Helicobacter pylori* infections [7] or cystic fibrosis (either using azithromycin or clarithromycin) may experience weight gain [8].

Probiotics, specifically some *Lactobacillus* species can also cause weight gain in farm animals [9]. They are commonly used

as growth promoters in Europe, where antibiotics are no longer allowed [3,10]. A study on mice, after ingestion of *Lactobacillus ingluviei*, has identified weight gain, an abnormal glucidic response and significant changes in the microbiota composition [11]. There is now congruent evidence that some probiotics have a similar effect and promote weight gain among young children [9]. A meta-analysis has shown that several species have a specifically higher potential as growth promoters in human and animals: *L. ingluviei*, *Lactobacillus fermentans*, *Lactobacillus acidophilus* and perhaps *Lactobacillus reuteri*. Some of these species are present in large numbers in some food or functional food marketed for humans [12]. Interestingly many *Lactobacillus* species secrete compounds with antibiotic activities [12]. Clearly, there is a link between antibiotic and probiotic activities.

Overall, this new field, combining obesity and gut microbiota manipulation, requires more investment from our field. Whenever possible, these studies need to be independent from the pharmaceutical companies and from the food industry to avoid biases of publications reporting [13]. In practice, we need to investigate the consequences of antibiotic treatments on our patients' weight. We need to investigate if probiotics added to the diets of young children play a role in obesity. We also need to develop scientific studies in collaboration with specialists in obesity. In the current issue, this journal is proposing a thematic approach comprising five reviews devoted to this topic: 'Gut Bacterial Microbiota and Obesity' by Mical *et al.* [14], 'Lessons from farm industry/probiotics' by Vernoux and Bernardeau [15], 'Obesity, non-alcoholic fatty liver disease and atherothrombosis: a role for the intestinal microbiota?' by Nieuwdorp *et al.* [16] and 'Gut microbiota and non alcoholic fatty liver disease: new insights' by Dutour *et al.* [17]. This link created between clinical microbiology and obesity may be very fruitful.

## Transparency Declaration

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## References

1. Ley RE, Turnbaugh PJ, Klein S, Gordon JL. Microbial ecology: human gut microbes associated with obesity. *Nature* 2006; 444: 1022–1023.
2. Koren O, Goodrich JK, Cullender TC et al. Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell* 2012; 150: 470–480.
3. Raoult D. Human microbiome: take-home lesson on growth promoters? *Nature* 2008; 454: 690–691.
4. Cho L, Yamanishi S, Cox L et al. Antibiotics in early life alter the murine colonic microbiome and adiposity. *Nature* 2012; 488: 621–626.
5. Trasande L, Blustein J, Liu M, Corwin E, Cox LM, Blaser MJ. Infant antibiotic exposures and early-life body mass. *Int J Obes (Lond)* 2013; 37: 16–23.
6. Thuny F, Richet H, Casalta JP, Angelakis E, Habib G, Raoult D. Vancomycin treatment of infective endocarditis is linked with recently acquired obesity. *PLoS ONE* 2010; 5: e9074.
7. Lane JA, Murray LJ, Harvey IM, Donovan JL, Nair P, Harvey RF. Randomised clinical trial: *Helicobacter pylori* eradication is associated with a significantly increased body mass index in a placebo-controlled study. *Aliment Pharmacol Ther* 2011; 33: 922–929.
8. Pirzada OM, McGaw J, Taylor CJ, Everard ML. Improved lung function and body mass index associated with long-term use of Macrolide antibiotics. *J Cyst Fibros* 2003; 2: 69–71.
9. Million M, Angelakis E, Paul M, Armougom F, Leibovici L, Raoult D. Comparative meta-analysis of the effect of *Lactobacillus* species on weight gain in humans and animals. *Microb Pathog* 2012; 53: 100–108.
10. Raoult D. Probiotics and obesity: a link? *Nat Rev Microbiol* 2009; 7: 616.
11. Angelakis E, Bastelica D, Ben AA et al. An evaluation of the effects of *Lactobacillus ingluviei* on body weight, the intestinal microbiome and metabolism in mice. *Microb Pathog* 2012; 52: 61–68.
12. Nagpal R, Kumar A, Kumar M, Behare PV, Jain S, Yadav H. Probiotics, their health benefits and applications for developing healthier foods: a review. *FEMS Microbiol Lett* 2012; 334: 1–15.
13. Ritchie ML, Romanuk TN. A meta-analysis of probiotic efficacy for gastrointestinal diseases. *PLoS ONE* 2012; 7: e34938.
14. Million M, Lagier J-C, Yahav D, Paul M. Gut bacterial microbiota and obesity. *Clin Microbiol Infect* 2013; 19: 305–313.
15. Bernardeau M, Vernoux J-P. Overview of differences between microbial feed additives and probiotics for food regarding regulation, growth promotion effects and health properties and consequences for extrapolation of farm animal results to humans. *Clin Microbiol Infect* 2013; 19: 321–330.
16. Knaapen M, Kootte RS, Zoetendal EG et al. Obesity, non-alcoholic fatty liver disease and atherothrombosis: a role for the intestinal microbiota? *Clin Microbiol Infect* 2013; 19: 331–337.
17. Aron-Wisnewsky J, Gaborit B, Dutour A, Clement K. Gut microbiota and non-alcoholic fatty liver disease: new insights. *Clin Microbiol Infect* 2013; 19: 338–348.